## Regulation of self-renewal and pluripotency by Sox2 in human embryonic stem cells.

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**Public Summary:**

**Scientific Abstract:**
Human embryonic stem (hES) cells, derived from blastocysts, are capable of unlimited self-renewal and differentiation into all cell lineages of the body. Because of their pluripotent nature, hES cells are valuable tools for understanding human development and advancing the field of regenerative medicine. However, one key to harnessing the therapeutic power of hES cells for biomedical applications begins with determining how these cells maintain their pluripotent and undifferentiated state. Studies in mice have implicated three factors in regulating pluripotency in embryonic stem cells, Oct4, Nanog, and Sox2. However, significant differences in growth regulation between mouse embryonic stem and hES cells have been identified, suggesting a need to determine when and how factors work in hES cells. To date, the transcription factors Oct4 and Nanog have been identified as critical regulators of stem cell fate by functional studies in hES cells. To determine the role of Sox2 in maintaining hES cell pluripotency and self-renewal, we used RNA interference to specifically knock down Sox2 gene expression. Reduction of Sox2 expression in hES cells results in loss of the undifferentiated stem cell state, as indicated by a change in cell morphology, altered stem cell marker expression, and increased expression of trophectoderm markers. In addition, knockdown of Sox2 results in reduced expression of several key stem cell factors, including Oct4 and Nanog, linking these three factors together in a pluripotent regulatory network. Disclosure of potential conflicts of interest is found at the end of this article.